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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/509,252	07/25/2005	Shunichi Kuroda	12480-000069/US	1324

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EXAMINER	
HORNING, MICHELLE S	
ART UNIT	PAPER NUMBER
1648	
MAIL DATE	DELIVERY MODE
08/11/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/509,252	KURODA ET AL.	
	Examiner	Art Unit	
	MICHELLE HORNING	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 May 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,6 and 8-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,6 and 8-13* is/are rejected.

7)☒ Claim(s) *8-13* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/6/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This action is responsive to communication filed 5/6/2008. The status of the claims is as follows: claims 1, 6 and 8-13 are under current examination.

Withdrawn Rejection

The 35 USC 102 (b) (Hildt) has been withdrawn due to claim amendments.

Claim Objections-NEW, NECESSITATED BY AMENDMENT

Claims 8 and 13 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Note that claim 1 limits the gene to an HSV1tk gene, while dependent claim 8 can be any gene. Claim 13 depends from claim 8.

Applicant is advised that should claims 1 and 6 be found allowable, claims 9-12 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Rejections - 35 USC § 112-NECESSITATED BY AMENDMENT

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 8 and 13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 8 recites the limitation "hepatic disease-treating substance" in claim 1. There is insufficient antecedent basis for this limitation in the claim. Claim 13 depends from claim 8.

Also it is not clear whether the "gene" in claim 8 refers to an additional gene to the HSV1tk of claim 1 or it refers to the same HSK1tk gene. Appropriate correction is required.

Claims 1, 6 and 8-13 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for at best HBsAg-HSV1 tk particles (defined by Figure 3) and treatment of a human hepatic cancer-derived tumor into rats, does not reasonably provide enablement for nanoparticles of all possible hepatitis B virus surface antigens and treatment of hepatic cancer in humans (see claims 1 and 6). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the

invention commensurate in scope with these claims. Enablement was considered in view of the *Wands* factors.

Response to Arguments

Applicant's arguments filed 5/6/2008 have been fully considered but they are not persuasive. In response to the above rejection, Applicants narrowed the claims so that the nanoparticle comprises a hepatitis B virus surface-antigen protein, the hepatic disease being treated is hepatic cancer in humans and the encapsulated substance includes an HSV1tk gene derived from simple herpes virus. Applicants provided Appendix A containing the published work of the Inventors demonstrating the effect of this drug in rat models which compared that to control. While Applicants have successfully addressed the lack of control in the specification demonstrating the effect of this drug in rat models, Applicants failed to address the treatment of hepatic cancer in humans. This is not supported by the instant specification. It is understood that such a drug is not cancer cell specific and would affect the entire liver as a whole.

Further, note that Applicants merely provide a single nanoparticle in the instant specification which does not commensurate with the scope of the claims. Structurally, the specification merely provides support for L antigen-forming nanoparticles (as defined by Figure 3) and not for all possible hollow nanoparticles with an HBVsAg protein. The ordinary artisan would not know how to make a hollow nanoparticle, if possible, by using the M or S antigen or any other protein having an HBVsAg, for example. Applicants have not demonstrated a correlation based on structure to function that would allow the ordinary artisan to make such a hollow nanoparticle that would

allow the specific claimed function. Without working examples, predictability in the art, a correlation of structure to function and sufficient guidance in the specification, there would be much undue experimentation required for the ordinary artisan to both make and use the full scope of the claimed invention. This rejection is maintained.

Claim Rejections - 35 USC § 103-MAINTAINED

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over the combined teachings of Hidlt and Xiang-Ling et al (2001).

Applicant's arguments filed 5/6/2008 have been fully considered but they are not persuasive. In response to the above rejection, Applicants argue that Hildt "merely

discloses that modified HBV vectors bind to hepatic cells" (see REMARKS, page 7) and that Xiang-Ling "merely shows the pharmacologic effect of the HSV-TK gene" (see REMARKS page 8). It appears that Applicants misinterpreted the teachings by Hildt. Hildt teaches a nucleic acid-containing particle, the particle comprising proteins, which can bind specific cells and introduce their nucleic acid into these cells, including liver cells (see paragraph 8, Summary of the invention, Abstract and paragraph 4, Background of the invention). The nucleic acids are "packaged" into the particle (see paragraph 16, Summary of invention).

Xiang-Ling et al disclose the killing effects of ganciclovir (GCV) on cells transduced with the HSV1-TK gene both *in vitro* and *in vivo* (see title). Cells transfected with the HSV1-TK gene are sensitive to GCV, a nontoxic antiviral drug (see Introduction). The authors demonstrate that the sensitivity of cells transfected with TK gene to GCV was 46 times higher than that of the parental cell (see Abstract). Further, the authors note that "much literature previously reported that the sensitivity of transfected cells to GCV was enhanced 102-103 times than that of parental cells" (see page 904). It would have been obvious to one of ordinary skill in the art to combine the teachings of Hidlt and Xiang-Ling et al in order to make a particle specifically containing the HSV-TK gene. One would have been motivated to do so in order to target a specific cell (e.g. liver cell by HBV), introduce the HSV-TK gene and administer GCV in order to kill specific cells. There would have been a reasonable expectation of success, given the teachings of Xiang-Ling et al demonstrate the sensitivity of cells transfected with TK gene to GCV was 46 times higher than that of the parental cell (see Abstract). The

invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made. This rejection is maintained.

Double Patenting-MAINTAINED

Applicants note that action will be taken at a later time with respect to the rejections below. Thus, these rejections are maintained.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-5 and 8 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 2 of copending Application No. 10/509247 (PG Pub 20050181064). Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to nearly identical products. More specifically,

they are drawn to a hollow nanoparticle with the ability to recognize a hepatocyte and it encapsulates a substance.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-6 and 8-13 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 3, 4, 6, 8-12 of copending Application No. 10/509248 (PG Pub 20060165726). Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to nearly identical products. More specifically, they are drawn to a hollow nanoparticle with the ability to recognize a hepatocyte and it encapsulates a substance. Further, the drugs are intravenously administered to humans.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-6 and 8-13 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 8 and 14-16 of copending Application No. 10/509249 (PG Pub 20060088536). Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to nearly identical products. More specifically, they are drawn to a hollow nanoparticle with the ability to recognize a hepatocyte and it encapsulates a substance. Further, the drugs are intravenously administered to humans.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-3 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 4 and 9 of copending Application No. 10/529749 (PG Pub 20060292118). Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to nearly identical products. More specifically, they are drawn to a hollow nanoparticle with the ability to recognize a hepatocyte and it encapsulates a substance.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MICHELLE HORNING whose telephone number is (571)272-9036. The examiner can normally be reached on Monday-Friday 8:00-5:00 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michelle Horning/
Examiner, Art Unit 1648

/Zachariah Lucas/
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